

Appl. No. 09/665,852  
Response Dated: September 21, 2004  
Reply to Office Action of June 21, 2004

P 1-9, 11, 12, 14, 15, 17-20, 28-30  
C-10, 13, 16, 21-27  
A-9, 11, 17  
N 28, 29, 30

### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

#### Listing of Claims:

Claim 1 (Previously presented): A mammalian host cell useful for producing rAAV in the absence of a helper adenovirus comprising:

- (a) a transgene under the control of regulatory sequences directing expression thereof and flanked by AAV inverted terminal repeats;
- (b) an AAV *rep* sequence and an AAV *cap* sequence under the control of regulatory sequences directing expression thereof; and
- (c) adenovirus sequences consisting of the minimum adenovirus DNA required to express an E1a gene product, an E1b gene product, and an E2a gene product, wherein the only adenovirus gene products expressed in the host cell are adenovirus E1a, E1b and E2a.

Claim 2 (Original): The host cell according to claim 1 wherein said transgene regulatory sequences comprise a promoter selected from the group consisting of a native promoter of the transgene, an inducible promoter, a tissue-specific promoter and a constitutive promoter.

Claim 3 (Previously presented): The host cell according to claim 1, wherein said DNA which expresses said E1a gene product is operably linked to a first promoter directing the expression of said E1a gene product;

said DNA which expresses said E1b gene product is operably linked to a second promoter directing the expression of said E1b gene product; and

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said DNA which expresses said E2a gene product is operably linked to a third promoter directing the expression of said E2a gene product.

Claim 4 (Original): The host cell according to claim 3, wherein said first promoter is selected from the group consisting of a native promoter of E1a, an inducible promoter and a constitutive promoter; wherein said second promoter is selected from the group consisting of a native promoter of E1b, an inducible promoter and a constitutive promoter; and wherein said third promoter is selected from the group consisting of a native promoter of E2a, an inducible promoter and a constitutive promoter.

Claim 5 (Original): The host cell according to claim 3, wherein said first promoter and said third promoter are not identical.

Claim 6 (Original): The host cell according to claim 3, wherein said first promoter and said third promoter are identical.

Claim 7 (Original): The host cell according to claim 3 wherein said first promoter and said third promoter are inducible promoters.

Claim 8 (Original): The host cell according to claim 3 wherein said first promoter or said third promoter is an inducible promoter.

Claim 9 (Currently amended): The host cell according to claim 1, wherein said transgene of (a) is stably integrated into the ~~chromosomes~~chromosome of said host cell, present in said host cell as an episome, or transiently expressed in said host cell;

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said AAV *rep* and *cap* genes of (b) are stably integrated into the ~~chromosomes~~chromosome of said host cell, present in said host cell as an episome, or transiently expressed in said host cell; and

said DNA of (c) is stably integrated into the chromosome of said host cell, present in said host cell as an episome, or transiently expressed in said host cell.

~~Claim 10 (Canceled).~~

Claim 11 (Currently amended): The host cell according to claim 1, wherein said transgene is supplied to said host cell by ~~[[an]]~~a rAAV.

Claim 12 (Original): The host cell according to claim 1, wherein said transgene and said DNA required to express said E1a gene product and said E1b gene product are supplied to said host cell on the same vector.

~~Claim 13 (Canceled).~~

Claim 14 (Previously presented): A method for producing recombinant adeno-associated virus (rAAV) in the absence of contaminating helper virus or wild-type virus, comprising the step of culturing the host cell of claim 1, wherein the only adenovirus gene products expressed in the host cell are adenovirus E1a, E1b and E2a.

Claim 15 (Original): The method according to claim 14, further comprising the step of purifying the rAAV from said host cell or host cell culture.

~~Claim 16 (Canceled).~~

Claim ~~17~~ (Currently amended): The method according to claim 15, wherein  
said minimum adenovirus DNA required to express an E1a gene product  
is operably linked to a first promoter selected from the group consisting of an inducible  
promoter, a constitutive promoter and a native promoter for E1a;  
said minimum adenovirus DNA required to express an E1b gene product  
is operably linked to a second promoter selected from the group consisting of an  
inducible promoter, a constitutive promoter and a native promoter for E1b; and  
said minimum adenovirus DNA required to express an E2a gene product  
is operably linked to a third promoter selected from the group consisting of an inducible  
promoter, a constitutive promoter and a native promoter for E2a.

Claim ~~18~~ (Original): The method according to claim 17, wherein at least one  
promoter of said first promoter, second promoter or third promoter is an inducible  
promoter, further comprising the step of adding to said host cell culture a first inducing  
agent to induce said inducible promoter.

Claim ~~19~~ (Original): The method according to claim 17, wherein said first and  
third promoters are different inducible promoters directing the expression of each  
respective gene product.

Claim ~~20~~ (Original): The method according to claim 19 further comprising the  
steps of adding to said host cell culture a first inducing agent for inducing said first  
inducible promoter and a second inducing agent for inducing said second inducible  
promoter, [whereby the ratio of expressed gene products may be varied for optimizing the  
production of rAAV in said host cells.]

~~Claims 21-27 (Canceled)~~

product by process  
or composition comprising  
rAAV & Host Cells

Claim 28 (New): A preparation of recombinant adeno-associated virus (rAAV) absent contaminating helper virus or wild-type virus in the presence of host cells comprising:

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- (i) a transgene under the control of regulatory sequences directing expression thereof and flanked by AAV inverted terminal repeats;
- (ii) an AAV *rep* sequence under the control of regulatory sequences directing expression thereof;
- (iii) an AAV *cap* sequence under the control of regulatory sequences directing expression thereof; and
- (iv) adenovirus sequences consisting of the minimum adenoviral DNA required to express an E1a gene product, an E1b gene product, and an E2a gene product, wherein the only adenovirus gene products expressed in the host cell are adenovirus E1a, E1b and E2a.

Claim 29 (New): The preparation of claim 28, wherein the adenovirus gene products are transiently produced in the host cell.

Claim 30 (New): The preparation of claim 28, wherein the adenovirus gene products are delivered via a plasmid.